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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
BRUMBACK, B	
ART UNIT	**PAPER NUMBER**
1642	13

DATE MAILED: 11/07/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/230,955	Applicant(s) MASON ET AL.	
	Examiner Brenda G. Brumback	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 August 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7 and 8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *5 and 7* is/are allowed.

6)☒ Claim(s) *1-4 and 8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is responsive to the amendment filed 08/27/2001. Claims 1, 3, 4, and 8 were amended. Claims 1-5, 7, and 8 are pending.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102

3. The rejection of claims 1 and 2 under 35 U.S.C. 102(b) as being anticipated by Porta et al. is maintained. Applicant's arguments have been fully considered but they are not persuasive. Applicant states that Porta uses the plural "monoclonal antibodies" in the general sense and does not teach two or more antibodies used on the same cervical smear sample. Applicant, however, has provided no further argument or evidence in support of this statement. Absent some evidence to the contrary, the plural antibodies disclosed by Porta are equivalent to a panel of two or more. Argument in the absence of evidence is not persuasive.

4. The rejection of claims 1 and 2 under 35 U.S.C. 102(b) as being anticipated by Kamiya et al., is withdrawn pursuant to applicant's amendment thereof and arguments, which were persuasive.

5. The rejection of claims 1 and 2 under 35 U.S.C. 102(b) as being anticipated by any of Smedts et al. is maintained. Applicant's arguments have been fully considered but they are not persuasive for the following reasons.

Applicant argues that Smedts et al. teaches contacting cervical tissue samples with a panel of monoclonal antibodies in contrast to applicant's claims, which have been amended to recite contacting cervical smear samples with a panel of monoclonal antibodies. Applicant argues that the samples used are different, in that a smear sample is simply a collection of cells, whereas a tissue sample is a coherent portion of tissue which has kept its original structure. However, absent some evidence to the contrary, the cervical tissue specimens disclosed by Smedts would encompass a collection of cells from the cervix. Applicant has provided no evidence that the cervical biopsy specimens disclosed by Smedts would not have been interpreted by one of ordinary skill in the art at the time the invention was made to have been equivalent to or the same as applicant's cervical "smear" sample, which applicant has defined in the response as a collection of cervical cells.

Applicant argues that Smedts does not demonstrate a "marker" that differs between premalignant or neoplastic cells. In response to applicant's argument that the references fail to show certain this feature of applicant's invention, it is noted that the feature upon which applicant relies (i.e. differentiation between premalignant or neoplastic cells,) is not recited in the rejected claims. Rather, the claims recite "a method for screening for a premalignant or neoplastic disease in a cervical smear sample". There is no recitation of differentiation between

premalignant and neoplastic disease states. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant argues that Smedts does not teach or suggest distinguishing normal cervical cells from premalignant or neoplastic cervical cells. Smedts, however, does compare antigens in normal, premalignant, and neoplastic samples using a panel of monoclonal antibodies to detect specific cellular antigens associated with metaplastic or malignant potential of cervical epithelia. See page 403, column 2, first paragraph, wherein Smedts discloses,

> "By using specific monoclonal antibodies directed against individual keratin polypeptides, it is possible to study changes in the type of epithelial differentiation in premalignant and malignant cervical lesions".

Thus, Smedts clearly teaches distinguishing premalignant and neoplastic cells from normal cells.

Nevertheless, even if Smedts did not teach or suggest distinguishing normal cervical cells from premalignant or neoplastic cells using the disclosed method, Smedts anticipates the claimed method by teaching the specifically recited method steps, *i.e.*, contacting a panel of two or more monoclonal antibodies having specificities for different antigens with a cervical sample, determining the binding of the monoclonal antibodies, and comparing the binding with the pattern of binding in a normal sample. The preamble of the claims, "A method of screening for a premalignant or neoplastic disease state" is a statement of intended use of the claimed method. If the body of the claim fully and intrinsically sets forth all of the limitations of the claimed method, and the preamble merely states, for example, the purpose or intended use of the

invention, then the preamble is not considered a limitation and is of no significance to claim construction (MPEP 2112.02).

Claim Rejections - 35 USC § 102/103

6. The rejection of claim 8 under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over either of Kerr et al. or Kamiya et al., is withdrawn pursuant to applicant's amendment.

The rejection of claim 8 under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over either of Porta et al., or Smedts et al. is maintained. Applicant's arguments have been fully considered but they are not persuasive for the following reasons. Applicant argues that claim 8 has been amended to recite an antibody which specifically competes with a monoclonal antibody according to claim 7, and as such non-specific binding mechanisms are not encompassed. However, applicant has failed to define the meaning of "specifically". The skilled artisan could reasonably interpret claim 8 as encompassing any monoclonal antibody which is directed against any antigen present in cervical tissue because the antibody would compete for binding sites with a monoclonal antibody according to claim 7.

Claim Rejections - 35 USC § 112

7. The rejection of claims 1-4 under 35 U.S.C. 112, first paragraph, is maintained. Applicant's arguments have been fully considered but they are not persuasive.

Applicant argues that the present invention uniquely identifies and uses antibodies that differ in their binding patterns between normal and disease cells. Applicant points to page 3, lines 9-19, page 4, lines 15-28, and Example 5 in support of this argument. Applicant further argues that the examples demonstrate a group of monoclonal antibodies that react differently with normal and abnormal cervical cells and that the claimed method utilizes a combination of antibodies with a characteristic binding pattern against normal cervical cells, which signals an abnormal sample when the pattern deviates. Lastly, applicant argues that methods of clinical diagnosis are not specifically set forth in the claims.

The portions of the disclosure referenced at pages 3 and 4 are general disclosures regarding the use of a panel of five monoclonal antibodies for detection of marker antigens on cervical and a general teaching that the pattern of binding of these antibodies differs in normal and abnormal cell samples. The data to support this disclosure is presented in Example 5, Tables 3 and 4. Firstly, it is somewhat difficult to interpret the data presented in Tables 3 and 4 because the meaning of the "ve" is not defined in either the disclosure or the footnotes. Secondly, Tables 3 and 4 disclose staining patterns of 10 normal samples and 10 premalignant specimens with a panel of 5 monoclonal antibodies, not 2 or more, as is claimed. Thirdly, it is not clear that the staining pattern of the premalignant specimens is significantly different from that of normal specimens in a significant number of specimens so as to be diagnostic of disease. A number of normal and premalignant specimens appear to be reactive with 9G5 and HG3 and unreactive with two or more of the remaining 3 MAB. There does not appear to be any data

whatsoever regarding differentiation of neoplastic specimens from normal specimens. Lastly, applicant's claims are drawn to a method of screening for a premalignant or neoplastic disease. Methods of clinical diagnosis of premalignant and neoplastic disease are clearly envisioned and encompassed within applicant's claimed method.

NEW GROUNDS OF REJECTION

Claim Rejections - 35 USC § 112

8. Claims 1, 2, and 4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection. Claim 1 has been amended to recite "each antibody having specificity for a different antigen of said sample relative to the other antibodies in said sample". This phrase does not appear to enjoy support in the specification. This matter might be resolved if applicant were to point out specifically where in the disclosure support for the newly recited material may be found.

9. Claims 1, 2, and 4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "in said sample" (line 4) in claim 1 renders the claim indefinite, as it would appear that it connotes that the antibodies are in the cervical smear sample, rather than the panel of monoclonal antibodies. Clarification and correction are required.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Smedts et al. The claims have been amended to recite a method of screening a cervical smear sample containing cells of the cervix comprising contacting a panel of two or more monoclonal antibodies with the sample, determining the pattern of binding of the monoclonal antibodies, and comparing the binding with the pattern of binding in a normal cervical smear sample. Smedts et al. teach a method of detecting cervical neoplasia and carcinoma comprising determining the binding of monoclonal antibodies directed against specific keratins in premalignant and malignant cervical tissue specimens and comparing the pattern of expression of the keratins in the specimens with the patterns of expression in normal cells (see the abstract and page 403, first paragraph). Although Smedts et al. teach staining cervical cells from biopsy specimens in a

retrospective study, one of ordinary skill in the art at the time the invention was made would have found it *prima facie* obvious to have applied the method disclosed by Smedts et al. for screening cervical smears for the presence of cells undergoing premalignant or neoplastic changes as a method of detecting abnormal cells in routinely collected cervical smears.

Conclusion

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Mattes et al. (U.S. Patent 4,666,845) teach a method of diagnosing cervical cancer comprising contacting cervical cells with a panel of monoclonal antibodies recognizing antigens associated with cancer (see the abstract; column 4, lines 16-24, and column 13, line 55, through column 14, line 18).

12. Claims 5 and 7 are allowable.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Brumback whose telephone number is (703) 306-3220. If the examiner can not be reached, inquiries can be directed to Supervisory Patent Examiner Anthony Caputa whose telephone number is (703) 308-3995. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Examiner Brenda Brumback, Art Unit 1642 and should be marked "OFFICIAL" for entry into prosecution history or "DRAFT" for consideration by the examiner without entry. The Art Unit 1642 FAX telephone number is (703)-305-3014. FAX machines will be available to receive transmissions 24 hours a day. In compliance with 1096 OG 30, the filing date accorded to each OFFICIAL fax transmission will be determined by the FAX machine's stamped date found on the last page of the transmission, unless that date is a Saturday, Sunday or Federal Holiday with the District of Columbia, in which case the OFFICIAL date of receipt will be the next business day.

Brenda Brumback
October 25, 2001